the Thebesian foramina of the septum, of at least some arterial blood. That this does not always suffice to maintain interventricular equilibrium, however, is illustrated by the dicrotic pulse, the pulsus paradoxus, and kindred phenomena.

Suggestive in this connection are the remarks of Professor Porter in his review of the subject of cardiac innervation in the "American Text-book of Physiology"[9]: "A positive demonstration that the nerve-cells in the heart are not essential to its contractions," says this observer, "is secured by removing the tip of the ventricle of the dog's heart and supplying it with warm defibrinated blood through a cannula tied into its nutrient artery. Long-continued, rhythmical, spontaneous contractions are thus obtained (Porter[10]). As the part removed contains no nerve-cells, the observed contractions can only arise in the muscular tissue, provided we make the (at present) safe assumption that the nerve-fibers do not originate impulses capable of inducing rhythmic muscular contractions." In other words,—and this may be said to apply to all muscular elements including those of the muscular coats of the stomach and intestines,—the cardiac muscle is endowed with the inherent power to contract, even small detached pieces, when placed in appropriate media being capable of doing so. In the body, indeed, this contractile power is merely, so to say, kept active, and Porter remarks—almost prophetically in the light of our views: "The demonstration that the nerve-cells are not essential to contraction places us one step nearer the true cause of contraction. It is some agency *acting on the contractile substance.*[11] Evidence is accumulating that this agent is a *chemical substance,* or substances, *brought to the contractile matter by the blood.*"

That the "chemical substance brought to the contractile matter by the blood" is represented by the adrenal secretion and the oxidizing substance seems clear. Brown-Séquard over fifty years ago urged that the inferior vena cava contained *some* undetermined substance which contributed to the heart's dynamism.

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[9] Porter: "American Text-book of Physiology," second edition, 1900.

[10] Porter: Journal of Experimental Medicine, vol. ii, p. 391, 1897.

[11] All italics are our own.

THE ACTION OF THE ADRENAL SECRETION AND THE OXIDIZING SUBSTANCE UPON THE CARDIAC MUSCLE.

The histology of the myocardium still offers a broad field for conjecture, notwithstanding the many investigations to which it has been submitted by modern observers. The known facts are briefly these: Its tissue is composed, in man, of short, round fasciculi, or bundles, of striated fibers, possessed of thick lateral projections. The latter directly connecting with a similar projection of the adjoining bundles and being cemented to it, a thick close-meshed net-work is formed: a characteristic of the heart-muscle. But it differs from other muscles in several other particulars; its fibers are one-third smaller and their striæ are much more faint; they possess no sarcolemma and are, therefore, exposed to the immediate action of any fluid that may surround them. The manner in which the contractile structures are combined in bundles is also peculiar: each bundle is made up of central prismatic fasciculi of round fibers, in which nuclei (one or two) with their surrounding protoplasmic area are imbedded, the whole being surrounded with flat or ribbon-like columns of muscle-fibers. The perinuclear protoplasm referred to generally contains fat-droplets and *minute pigment-granules* which resemble hæmoglobin, and sends projections between the surrounding muscular fibers so that each of the latter is connected with and is only separated from its neighbor by a layer of protoplasm. This arrangement does not in any way modify the manner in which the sarcous elements are disposed, while the disks, clear spaces, etc., are precisely as they are elsewhere in the organism. These muscular "primary" bundles form, by their union with one or two of their neighbors, columns, or chains—or "secondary" bundles, which are covered, as shown by Ranvier, with a sheath of loose connective-tissue cells, which cells, in turn, connect with one another by numerous projections, or extensions. The primary fasciculi also contain connective-tissue sheaths which invest the muscle-fibers and are likewise supplied with connective-tissue cells. All this forms a close, though permeable, net-work, which makes it possible for a liquid to penetrate the muscular columns or chains and come into direct contact with the bare, or exposed, muscle-fiber.

Indeed, the intimate structure of the myocardium precisely supplies the required structure for the equable and free distribution of such an agency as the suprarenal secretion represents. Fluids can penetrate through the maze of cellular tissue to the bare muscular fibers; the sheaths that include the columns or chains of muscular bundles afford a peculiar system of canalization through which the liquids can easily gain access to them. These canals—the lacunæ of Henle—are the intervals between the columns of secondary bundles, or their sheaths, rather, which are placed in longitudinal apposition. Schweigger-Seidel and Ranvier having observed that interstitial injections of colored substances penetrated the lymphatic vessels, the lacunæ have been considered as adjuncts, or extensions, of the latter.

Renaut,[12] however, concluded that the penetration of the colored fluids into the lymphatics merely demonstrated the weak resistance of the endothelial coat of the latter, and the spaces, or lacunæ, of Henle being unprovided with endothelial walls, there was no ground for the prevailing belief that they represented lymphatic vessels. He found that all the lymphatic capillaries of the myocardium are located on the surface of the heart underneath the pericardium. They are large and bosselated and form a mesh-work which covers the whole cardiac surface, and send smaller blind pouches into the muscular interstices. The spaces of Henle should be considered, he thinks, "not as true lymphatic cavities analogous to those observed around the pulmonary lobules of certain animals, but as mere connective-tissue spaces, which represent, in fact, pathways for lymph." In a foot-note Berdal states that the spaces of Henle are crossed by "vessels," and in the text the following remark as to the identity of this lymph appears: "The muscular fibers of the heart are thus bathed in connective-tissue spaces in which lymph easily circulates; but this lymph is not that of the lymphatic vessels or capillaries, but that of loose connective-tissue spaces (Renaut)." It is needless to state that this suggests the presence of blood-plasma. Still, we can only consider this deduction as tentative.

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[12] Renaut: Traité d'Histologie pratique, p. 719; quoted by Berdal, *loc. cit.*, p. 825.

The manner in which the blood-plasma, whether venous or arterial, is distributed by the Thebesian channels is well shown in a study of the vessels of the heart by Arthur V. Meigs.[13] The extreme paucity of literature on the Thebesian channels has caused them to be overlooked by practically all histologists; that they should be treated as capillaries in the author's paper is, therefore, as normal as it is for text-books to do so. "The capillaries of the human heart," says Dr. Meigs, "differ in two ways from those of other parts of the body: they penetrate the muscular fibers, and some of them are larger than those found elsewhere, and of different arrangement. . . . The accompanying illustrations are drawings which were made with the camera lucida. They are from sections of two human hearts. The first is from the heart of a negro woman, 40 years old, who died of burns. Some pieces of the organ were preserved in Fleming's solution, and others in 70-per-cent. alcohol, and they were stained in bulk with borax-carmine and imbedded in paraffin. The second heart is that of a man, 30 years old, who died of lead encephalopathy. When the post-mortem examination was made, the heart being still quite fresh, there was injected through each of the two coronary arteries as much as the blood-vessels would easily receive of a solution of 3 grammes of Berlin blue (Grübler's) in 600 cubic centimeters of water. Pieces of the organ of suitable size were at once placed in preservative fluid, some in 70-per-cent. alcohol, and others in formaldehyde solution. The tissue was afterward stained in bulk with borax-carmine and imbedded in paraffin.

"The penetration of the muscular fibers by the capillaries is made perfectly clear by the illustrations; it is shown as well by the injected as by the uninjected heart. The two methods of demonstration supplement one another, because, in injected tissue which has been stained, the blood-vessels and their situation are made very obvious by the contrast of color, but the details of the structure of the walls are obscured by the injection material, while, on the other hand, in the uninjected tissue, the structure of the blood-vessels can be seen with the utmost distinctness. In Figs. 1 to 4 the capillaries are easily recog-

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[13] Arthur V. Meigs: Journal of Anatomy and Physiology, Jan., 1899.

nized. Their situations in relation to the muscular fibers are very varied. Some are in the intermuscular fibers, others slightly indent the sides of the fibers; still others are within the fibers close to their peripheries, and sometimes the capillaries are in the very centers of the fibers. This penetration of the muscular fibers of the human heart in the adult is a most

DESCRIPTION OF DR. MEIGS'S PLATE.

The amplification has been reduced about one-third in the reproduction herein presented.

"Fig. 1.—x 420. From a man, 30 years old, who died of lead encephalop- *bb* are athy. A section of papillary muscle of the heart cut across the fibers. injected capillaries, the one partially and the other entirely within the muscular fibers. *c*, A capillary which remains uninjected; its nucleus is included.

"Fig. 2.—x 420. From the same tissue as Fig. 1. *v*, A vein stained by the injection material. *bb*, Capillaries whose precise situation cannot be defined. They cannot be said to be intermuscular spaces, nor to be entirely within fibers. The effect is as if the fibers were coalescing.

"Fig. 3.—x 420. From the same tissue as Fig. 1. *f*. A capillary in a fiber. *g*, A capillary in the center of a very small fiber. This is perhaps the most convincing instance of the penetration of a muscular fiber by a capillary.

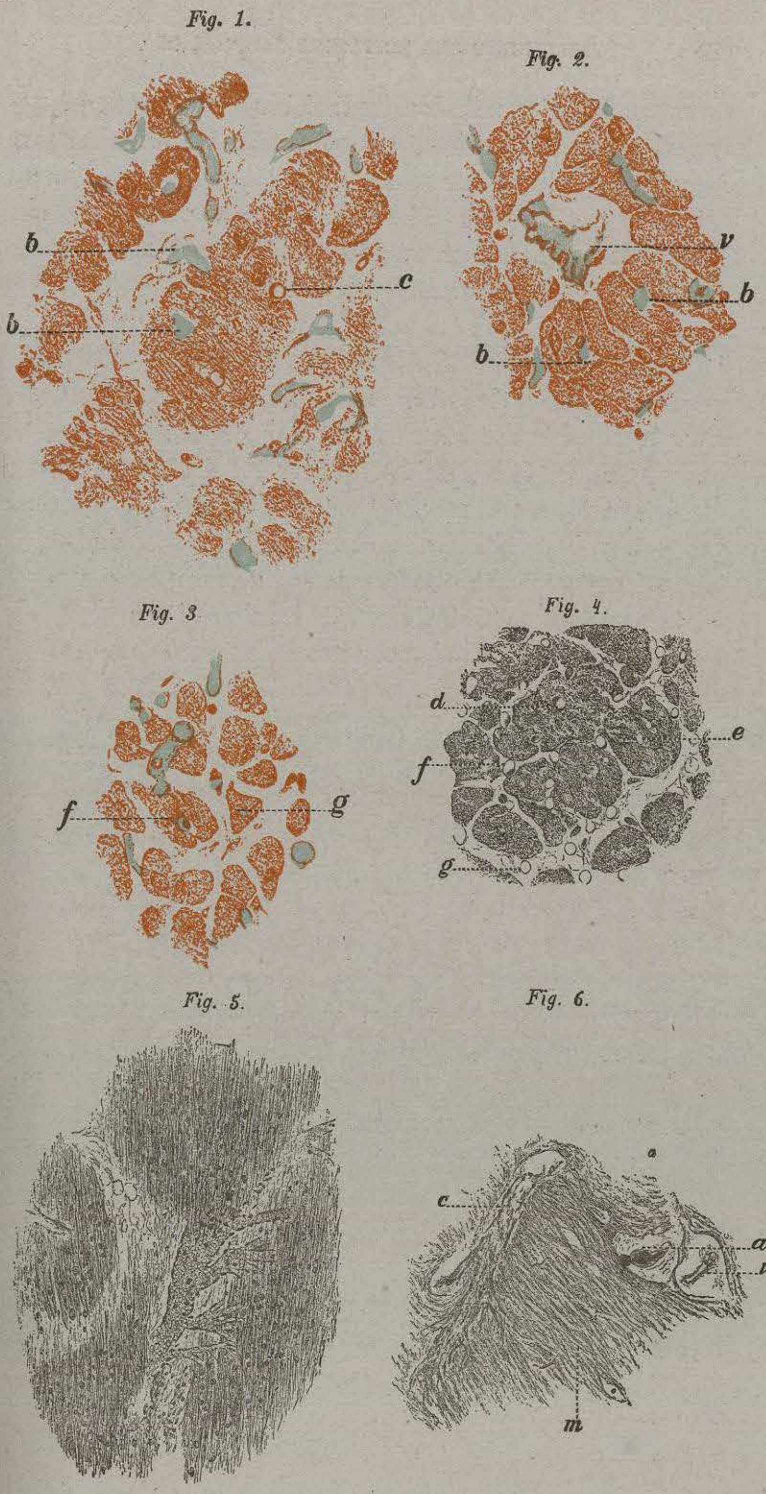
"Fig. 4.—x 420. A section of heart cut transversely to the muscular fibers, from a negro woman, 40 years old, who died of burns. The muscular fibers are of irregular shape. *d*, A capillary within a muscular fiber, its nucleus upon one side producing a resemblance to a seal ring. *e*, A capillary within a muscular fiber. *f*, A capillary in an intermuscular space; its nucleus being included, it resembles a seal ring. *g*, A capillary in an intermuscular space; its endothelial wall appears as a simple circle.

"Fig. 5.—x 115. From the same tissue as Fig. 4. A large capillary, receiving many branches and surrounded by muscular tissue. The capillary and its branches are almost filled with blood-corpuscles. The capillary walls are distinctly visible, containing many flattened endothelial nuclei.

"Fig. 6.—x 42. From the same tissue as Fig. 1. Not printed in two colors, because the essentials show equally well in black. *m*, Muscular tissue. *a*, An arteriole; the solid black within its caliber is injection material. *v*, The accompanying vein to the arteriole, *a*; it also contained a little of the injection material; these two vessels are in a connective-tissue interspace. *c*, A large capillary; it contains a good deal of the blue injection material, which is represented by the heavily-shaded portions. These three vessels—arteriole, vein, and capillary—give a good idea of the character of such vessels in the heart. The great size of the capillary is the most striking feature."

striking and curious phenomenon, and it does not exist at an early embryological stage. The condition is, therefore, one of later development, but it is not yet known at how early an age it does exist . . . .

"Very large capillaries are found in the human heart, and such vessels are shown by Figs. 5 and 6. It is not common to find minute veins in company with the arterioles in the deepest



CIRCULATION OF THE HUMAN HEART. *[Arthur V. Meigs.]*

[Journal of Anatomy and Physiology.]

portions of the muscular substance of the heart, although it is well known that, upon the surface and in the connective-tissue interstices, arteries are found with their venæ comites, just as they are in other organs and tissues. The arrangement of the vessels upon the surface and in the interstices is in marked contrast with that found in the muscular substance proper. Here, when an arteriole is accompanied by an efferent vessel, this vessel is single coated and composed of endothelium, being exactly like the smallest capillaries, except in size. These peculiar large capillaries are found not only in company with arterioles, and, therefore, when carrying on the function usually performed by veins, but also alone. When they are alone, it is impossible to be certain whether their function was afferent or efferent. It may well be that arterioles are less numerous in the heart than in other tissues, and that their place is taken by the large capillaries. These capillaries are so numerous and of such size that it seems likely they perform the function of reservoirs. The presence of the large capillaries and the penetration of the muscular fibers by the capillaries indicate a provision for the blood-supply of the heart even more bountiful than that of the other organs."

That these vessels are the Thebesian channels is evident; their mode of distribution and the peculiar endings of their subdivisions is particularly well shown in Fig. 6, while the outpouring of plasma for absorption by the muscle-elements is suggested by Fig. 5.

The fact that the distribution of the Thebesian channels is analogous to that observed in the heart of the frog has, we have seen, been noted by Pratt. This had also been noticed by Lannelongue, but this author considered the channels of the human myocardium as vestiges of the batrachian system. Berdal, who alludes to the latter, states that in the frog and in the batrachian *urodela* there are no ordinary blood-vessels. "The muscular fasciculi intercept cavernous spaces into which the blood penetrates directly and from which they are only separated by endothelium. *The frog's heart is thus a true sponge the structures of which, formed of muscular fibers, nourish themselves by imbibition.* In mammals, on the contrary, the myocardium contains distinct vessels. The capillaries form a net-work the meshes of which, elongated and parallel to the muscular fasciculi, are connected by short branches, which give each mesh the appearance of a parallelogram. When these vessels cross the spaces of Henle, they are covered, on the external surface, with flat connective-tissue plates." Pratt's observation not only includes the analogy between the human lung and that of the frog, but also with that of the cat, a mammal. Under these conditions, it becomes clear that in man, also, *the heart-muscle may be regarded as a sponge-like structure, the contractile elements of which are nourished and supplied with working energy by substances in the blood-plasma.*

What is the rôle of the blood of the coronary arteries in the functions of the heart? This may perhaps be traced by analyzing the effects of ligation of these arteries upon these functions. Porter[14] refers as follows to the experimental work in this connection: "The frequency of arrest after ligation is in proportion to the size of the artery ligated, and hence to the size of the area made anæmic, and is not in proportion to the injury done in the preparation of the artery. The circumflex and descendens may be prepared without injuring a single muscle-fiber, yet their ligation frequently arrests the heart, while the ligation of the arteria septi, which cannot be prepared without injuring the muscle-substance, does not arrest the heart. It is, moreover, possible to close a coronary artery without mechanical injury. Lycopodium-spores mixed with defibrinated blood are injected into the arch of the aorta during the momentary closure of that vessel and are carried into the coronary arteries: the only way left open for the blood. The lycopodium-spores plug up the finer branches of the coronary vessels. The coronary arteries are thus closed without the operator having touched the heart. Prompt arrest, with tumultuous fibrillary contraction, follows."

If the plasma that reaches the heart by way of the Thebesian channels can sustain both its nutrition and its contractions, how can such results as these be accounted for? The sudden arrest of the heart's action by plugging the coronary arteries certainly points to a predominating function, and, more than this, to a function of which they are alone the sources of blood-supply. That the rôle of the coronary blood is precisely that which obtains elsewhere in the organism is forcibly suggested by the experiments of Langendorff, who was able, according to Porter, "by circulating warmed *oxygenated defibrinated* blood through the coronary vessels, to maintain the hearts of rabbits, cats, and dogs in activity after their total extirpation from the body." It is clear that the blood-plasma can incite functional activity when introduced through the coronaries as well as when introduced into the ventricles. "Even pieces removed from the ventricle will contract for hours," continues the author, "if fed with blood through a cannula in the branch of the coronary artery which supplies them (Porter[15]). It is evident, therefore, that the cause of the rhythmic beat of the heart lies *within the heart itself,* and not within the central nervous system."

The italicized words represent precisely the factor of the problem which must be eliminated to enable us to differentiate the rôle of the coronary plasma from that of the Thebesian plasma, for blood will not alone induce contraction of the cardiac walls; almost any irritant will under appropriate conditions. Indeed, in the latter case it will sometimes undergo contractions without any external irritation; thus, "a strip of muscle cut from the *apex* of the tortoise ventricle and suspended in a moist chamber begins in a few hours to beat apparently of its own accord with a regular, but slow, rhythm, which has been seen to continue as long as thirty hours. If the strip is cut into pieces and placed on moistened glass slides, each piece will contract rhythmically. Yet in the apex of the heart no nerve-cells have been found" (Porter). Hence the power to contract is inherent in the contractile tissues, and subject, as elsewhere in the organism, to exacerbations of activity under appropriate stimulus. This fact being now established, our inquiry is simplified, since we need only to inquire into the nature of the processes through which it is utilized.

Analysis of the requirements of the right heart soon reveals the fact that the muscle-fibers require the same blood-supply that any muscle of the body does. Indeed, we then realize that the coronary arteries are their only source of oxy-

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[14] Porter: *Loc. cit.*

[15] Porter: Journal of Experimental Medicine, vol. ii, p. 391, 1897.

gen. The venous blood that reaches it through the Thebesian channels has been depleted of this gas by the rest of the organism, and the suprarenal secretion, owing to its marked avidity for it, must, while in transit through the inferior vena cava, have deprived it of the little that might have remained in loose combination. We have reviewed the ultimate distribution of the coronary arteries as given by Berdal. It does not differ from that of other text-books. These generally concur in stating that the larger branches are distributed to the connective tissue between the large fasciculi, and once therein divide into arterioles, which, in turn, subdivide into capillaries that entwine the primary muscle-fasciculi. "The capillaries of the myocardium are very numerous," say Böhm and von Davidoff, "and so closely placed around the muscle-bundles that each muscular fiber comes in contact with one or more capillaries." Do they serve here, as elsewhere, to supply the muscle-fiber with its *source of energy*—*i.e.*, the carbohydrates that enter into the formation of the myosinogen—besides furnishing the oxidizing substance which sustains the combustion processes when brought into contact with this myosinogen? This is precisely where a difference between the muscular functions of the heart and those of other muscular structures appears to us to exist.

There is practically no *passive* period in the heart's action when we consider that its stage of *activity* recurs every three-fourths of a sound; and the formation of myosinogen in its contractile elements, were it to proceed as slowly as it does elsewhere, would seem totally inadequate. Still, if the coronary blood is not endowed with the mission of supplying the heart-muscle with its source of energy, we are relegated to the venous blood of the Thebesian vessels and its suprarenal secretion for the myosinogen-forming products. A possible source of energy suggests itself when we consider that a carbohydrate known to react under the effects of the oxidizing substance is present in the hepatic veins,—*i.e.*, dextrose,—and that this sugar must pass through the right heart. As is well known, these veins carry their sugar to the inferior vena cava. That it is not used by the heart, however, was shown by a careful analysis of the whole question. This is submitted in the twelfth

chapter. For reasons submitted in the second volume I was led to conclude that the minute granules referred to on page 433 were actually supplied to the heart through the intermediary of leucocytes. These cells were found to migrate from the liver (also through the hepatic veins) to the inferior vena cava, where they meet the adrenal secretion and proceed with it to the right ventricle. The evidence seems incontrovertible. The subject is so far-reaching, however, that it had to be considered separately. I shall, for the present only, refer to these granulations as "granules β" (Ehrlich). We now have, it seems to me, the elements necessary to account for the functional phenomena witnessed, namely:—

1. *The adrenal secretion, to contract the right auricle and ventricle and thus insure the penetration of the Thebesian blood into the cardiac walls* (which contraction venous blood or its contained granules β would not cause).

2. *The granules β, to account for the unusual and continuous production of energy which the heart converts into work.*

3. *A continuous supply of oxidizing substance via the coronary arteries to insure the combustion processes through which this energy is liberated.*

The annexed colored plate shows the manner in which the adrenal secretion and the granules β simultaneously reach the right auricle.

We can now understand why plugging of the coronary arteries should, as stated by Porter, arrest cardiac action. Referring to the effects of embolism and thrombosis of these arteries, this investigator also says: "That part of the heart-wall supplied by the stopped artery speedily decays. The *bloodless area* is of a dull-white color, often faintly tinged with yellow; rarely it is red, being stained by *hæmoglobin* from the neighboring capillaries. The cross-section is *coarsely granular.* The nuclei of the muscle-cells have lost their power of staining. The muscle-cells are dead, and connective tissue soon replaces them. This loss of function and rapid decay of cardiac tissue would not take place did anastomosis permit the establishment of collateral circulation between the artery going to the part and neighboring arteries. . . . The objection that one of the coronary arteries can be injected from another, and that,